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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,380	03/12/2004	Viia Valge-Archer	08702.0137-00000	6499

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EXAMINER	
STOICA, ELLY GERALD	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/798,380	VALGE-ARCHER ET AL.	
	Examiner	Art Unit	
	Elly-Gerald Stoica	1467	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,15,23 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,15,23 and 38* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/18; 11/16/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Election/Restriction

1. Applicant's election without traverse of Invention I, claims 1-13,15, 23 and 38, drawn to an isolated antibody that binds to an IL- 21 receptor, and the following Sequence Ids. : SEQ ID NOs. 65-67 (e.g., for claim 1); SEQ ID NOs. 68-70 (e.g., for claim 4); and SEQ ID NOs. 71-73 (e.g., for claim 5); as well as the corresponding nucleotide and amino acid sequences in other claims grouped as Invention I, in the reply filed on September 6, 2006, is acknowledged.

Status of the claims

2. Currently claims 1-13,15, 23 and 38 are pending and being examined. Claims 14, 16-22, 24-37 are withdrawn from prosecution as being drawn to a non-elected invention.

Claims objections

3. Claim 23 is objected to as depending on a non-elected claim.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13,15, 23 and 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims contain the terms IL-21 Receptor and antibody to IL-21 Receptor. According to the specification (pages 19-20) the term IL 21 receptor is given a recitation of six possible definitions without adequate written description. For instance:

- the IL-21 receptor may be mammalian and has "an amino acid sequence of a naturally occurring mammalian IL-21R polypeptide or a fragment thereof, e.g., an amino acid sequence shown as SEQ ID NO: 43 (human) or SEQ ID NO: 45 (murine). However, description of SEQ ID NO: 43 and 45 is insufficient to the genus of "mammalian" IL-21R.

- the term "IL-21R" may refer to a receptor which is capable of binding to IL-21, and has an amino acid sequence substantially identical to, e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99% identical to, an amino acid sequence shown as SEQ ID NO: 43 (human) or SEQ ID NO: 45 (murine) or a fragment thereof. However, the specification only discloses SEQ ID NO: 43 and 45.

- the term "IL-21R" refers to a receptor which is capable of binding to IL-21, and has an amino acid sequence substantially identical to an amino acid sequence which is encoded by a naturally occurring mammalian IL-21R nucleotide sequence or a fragment thereof (e.g., SEQ ID NO: 44 (human) or SEQ ID NO: 46 (murine) or a fragment thereof. Is a protein 85% identical to the human sequence, to the mouse sequence, to a short fragment capable of binding to IL-21?

- the term "IL-21R" refers to a receptor which is capable of binding to IL-21, and has an amino acid sequence substantially identical to an amino acid sequence encoded by a nucleotide sequence which is substantially identical to, e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99% identical to, a nucleotide sequence shown as SEQ ID NO: 44 (human) or SEQ ID NO: 46 (murine) or a fragment thereof. Is a protein 85% identical to the human sequence, to the mouse sequence, to a short fragment capable of binding to IL-21?

- the term "IL-21R" refers to a receptor which is capable of binding to IL-21, and has a nucleotide sequence that hybridizes to one of the foregoing nucleotide sequences under stringent conditions, e.g., - highly stringent conditions. Two which sequence should it hybridize, to the whole sequence or to a fragment of it and how long should the fragment be?

Moreover, "the IL-21R may bind to IL-21 of mammalian origin, e.g., human or mouse". Should one understand that the binding is optional? Given such an array of alternative definitions one skilled in the art would not be able to envision the protein and therefore the antibody of the invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only claims related to murine and human IL-21 R, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

With regard to the antibody definition, the definition offered by the applicant that an antibody "encompasses any polypeptide comprising the antigen binding site" (page 16, [0042]), where an antigen binding domain could be an isolated complementarity determining region (CDR), contravenes with the accepted state of the art which shows that the antibody specificity is conferred by at least five if not the full complement of six

CDRs (figure 3.8, paragraph 3.6 as well as the Glossary, in chapter 3, Immunobiology, Janeway et al. eds., Garland publishing, New York, 2001, ISBN 081533642 X; also, US Pat. No. 5565332, col. 6, line 51-col. 7, line 11). Reduction to practice in effect provides the only evidence to corroborate conception (and therefore possession) of the invention.

Claims 1-13,15, 23 and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific antibody presented in the examples, does not reasonably provide enablement for the full scope of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Any other antibody to IL-21 receptor would not be enabling because the protein IL-21 R is so broadly described that, according to the written description, one skilled in the art would not have known to use the invention. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:
1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In the present case, the Applicant has provided a structural limitation for the antibodies (to comprise CDRs of a disclosed structure, or have certain amino acid sequences). Claims 4 and 5 refer to "conservative" amino acid substitution

in the CDRs. The role of the CDRs was well established in the art (in chapter 3, Immunobiology, Janeway et al. eds., Garland publishing, New York, 2001, ISBN 081533642 X) and a skilled artisan would have found very difficult to predict that a CDR mutated CDR, having even a "conservative" substitution would still bind to its known antigen. The specification does not provide any working examples with regard to the actual substitutions accepted by the CDRs while maintaining the binding to the IL-21 receptor, since the mere recitation of a list of "conservative substitutions" does not provide evidence that the actual 'Mutated antibodies " were actually binding to IL-21 Receptor. Even more, the protein IL-21 R is so broadly described that, according to the written description, one skilled in the art would not have known to use the invention beyond the working examples presented. A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13,15, 23 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Because the claims have, as a defining characteristic, binding to IL-21 R and since the IL-21 receptor is not adequately

described in the specification, the claims are indefinite because the antibody could not be envision without description of the antigen and thus the metes and bounds of the invention could not be determined. Moreover individual claims have supplementary problems, as follows:

- claims 4 and 5 contain the term "and conservative substitution thereof". Again, without further limitation the metes and bounds of the claim are indefinite.

- claim 15 recites "a pharmaceutical composition comprising an antibody". As presented, the claim is incomplete, since a composition must comprise at least two elements.

- claim 38 contains the term a diagnostic kit comprising the antibody..." As presented, the claim is incomplete, since a kit must comprise at least two elements and the relationship between the elements must be specified.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4, 5 8-13, 15 and 38 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hodge MR (WO200069880, 11/23/2000). The claims are drawn to an antibody having certain disclosed CDRs, antibody that binds at least 100 contiguous amino acids from the SEQ

ID NO 43 (i.e., the human IL-21 receptor sequence). Hodge MR claims (claim 11) an antibody that selectively binds to a polypeptide of SEQ ID NO 2 (that is the human IL-21 receptor). Hodge is silent about any particular CDRs. However, due to the breadth of the claims and since the specificity of the antibody is conferred by the CDR regions, it appears that the antibody of Hodge would have contained at least a number of the CDR regions enumerated in the instant application and therefore anticipate or make obvious the antibody of the claims in the instant application.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elly-Gerald Stoica whose telephone number is (571) 272-9941. The examiner can normally be reached on 8:30-17:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER